



PA (AMRA-) AMRAD OPERATIONS PTY LTD.  
 XX Vaux DL;  
 XX WPI: 1997-350966/32.  
 DR N-PSDB: AAT72711.  
 XX  
 PT Isolated protein homologues of viral inhibitors of apoptosis - used  
 PT to modulate apoptosis for treatment of degenerative, infectious or  
 PT autoimmune diseases and cancer  
 XX  
 PS Claim 8: Page 51-54; 136pp; English.  
 XX  
 CC Mammalian IAP homologue B (MIIB) (AAW19746) is a human homologue of  
 CC baculovirus inhibitor of apoptosis protein (IAP). Its amino acid  
 CC sequence was deduced from a cDNA clone (see also AAT72711). Isolated  
 CC from a human foetal liver cDNA library using primers based on  
 CC human EST sequences that resembled the BIR repeats of Oryza  
 CC pseudotsugata polyhedrosis virus IAP. IAP homologues (see also  
 CC AAW19745 and AAW19747-52) and their derivatives and chemical analogues  
 CC can be used in methods for modulating apoptosis in animal cells,  
 CC specifically for treatment, by inhibition, of degenerative and  
 CC infectious disease or, by promotion, of cancer and autoimmune  
 CC disease.  
 CC  
 XX  
 XX  
 SO Sequence 618 AA;  
 Query Match 100.0%; Score 3277; DB 18; Length 618;  
 Best local similarity 100.0%; Pred. No. 1.3e-289;  
 Matches 618; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 MHKTSQRLFPGPSYONIKSIMEDSTILSDWTNSNKKMKYDPSCELYRMSYTFEPAGY 60  
 DB 1 mhktasqrlfpgpsyqnklsimedstilsdwtcnankqkmydfscelyrmsytfepgy 60  
 QY 61 PVSESLARAGFYTYGVNDKVKFCGGLMDNMKLGDSPIQKHQLYPSCSFIONLYVAS 120  
 DB 61 pveselarsagfyytygvndkvkfcgglmndmwlqgsdpsqkqklypscstfionlyvas 120  
 QY 121 LGSTSKNTSPMRNSFAHSLSPTLHSSLFSGSYSSLSPPNLNSRAVEDISSRTNPSYA 180  
 DB 121 lgstskntspmrnsfahslsptlhsslfsgysaislspnlnsravedissrtcnpsya 180  
 QY 181 MSTEERARLYTHMWPRLFSPSLARAGFYTYIGGDNVACFACGGKLSMWEKXDMASEH 240  
 DB 181 msteearllythmwprlfslpselaragfyyiggnvactacggklsmwepkddamseh 240  
 QY 241 RHPFNCPLFENSLFETLRFSTISLKSQTTHAAMRTFMWSSVVPQEQLASAGFYVGR 300  
 DB 241 rthfncplfenslfetlrfstislsmqthaaemrtfmwpsvvpqeqlaasagfyyvgr 300  
 QY 301 NDVAVCFCCDGLKWCESGDDPWVBNHAKWFPCEFLIRMGQEFVDEIDGRYPHLEQL 360  
 DB 301 ndvavcfccdgglrcwesgddpwvbnhkwfprceflirmgqefvdeidgryphlleql 360  
 QY 361 STSDTFGEENADPPIHFGGSESSSEDVMMNTPVKSALEMGFNRDLVKOTVQSKILTT 420  
 DB 361 stsdctgeenadpplihfpgseessedavmmntpvrksalemgfnrdlvkqvsgkiltt 420  
 QY 421 GENVYNDIVSALINDEKREERKQAEEMASDDLIRKNHVALQOULTCVLPITD 480  
 DB 421 genylvndivsalinadekreerekqaeemasddslirnmahlequltcvlpitld 480  
 QY 481 NILKANVINKEOHIIKOKOTPLQARELIDPIIYKNAANAIFKCKLEIDNSTLYKRLF 540  
 DB 481 nilkanvinkeohiikokotplqarelidpiilvknanaaifkckleidscllykrlf 540  
 QY 541 VKNKKKTYPTEDVSGLSLEQLRLLOEBRTKVCMDKESVVFIPCGHLVVCQECAPSLR 600  
 DB 541 vkknkkytptedvsglsleqlrlloebertkvcmdkesvvpfpcghlvvcqecapslr 600  
 QY 601 KCPICRGIIKGVTRFELS 618

DB 601 kcpicrgiikgvtrfels 618  
 RESULT 2  
 AAW13545  
 ID AAW13545 standard; protein: 618 AA.  
 XX  
 AC AAW13545;  
 XX  
 DF 22-JUL-1997 (first entry)  
 XX  
 DE Human C-IAP1.  
 XX  
 KW IAP, inhibitor; apoptosis; RING finger domain; restlinosis;  
 KW myocardial infarction; nephritis; HIV.  
 XX  
 OS Homo sapiens.  
 XX  
 PN WO9706182-A1.  
 XX  
 PD 20-FEB-1997.  
 XX  
 PF 06-AUG-1996; 96WO-US12860.  
 XX  
 PR 08-DEC-1995; 95US-0569749.  
 PR 08-AUG-1995; 95US-0512946.  
 XX  
 PA (TULAR-) TULARIK INC.  
 XX  
 PI Goeddel DV, Rothe M;  
 DR WPI: 1997-154209/14.  
 DR N-PSDB: AAT61590.  
 XX  
 PT Nucleic acids encoding cellular inhibitor of apoptosis proteins  
 PT useful for apoptosis regulation in cells to reduce or increase  
 PT apoptosis and for pharmacological screening  
 XX  
 PS Disclosure: Page 18-20; 35pp; English.  
 CC The human cellular inhibitor of apoptosis proteins (C-IAP1/2 -  
 CC AAT61590/761591) comprise a series of defined structural domain  
 CC repeats and/or a RING finger domain. In particular, at least two of  
 CC a first domain repeat (AAW13547 or AAW13548), a second domain repeat  
 CC (AAW13549 or AAW13550), and a third domain repeat (AAW13551 or AAW13552)  
 CC and/or a RING finger domain (AAW13553 or AAW13554), or a consensus  
 CC sequences derived from these human genes.  
 CC The nucleic acid is used for recombinant prodn. of human cellular  
 CC inhibitor of apoptosis protein which modulates apoptosis  
 CC regulation. The nucleic acids are useful in therapies where  
 CC increased cell-specific apoptosis is desired, e.g. in restlinosis,  
 CC inflammatory disease states, myocardial infarction, glomerular  
 CC nephritis, transplant rejection and infectious diseases, e.g. HIV.  
 CC They can also be used in conditions requiring a reduction in  
 CC apoptosis.  
 CC  
 XX  
 SO Sequence 618 AA;  
 Query Match 100.0%; Score 3277; DB 18; Length 618;  
 Best local similarity 100.0%; Pred. No. 1.3e-289;  
 Matches 618; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 MHKTSQRLFPGPSYONIKSIMEDSTILSDWTNSNKKMKYDPSCELYRMSYTFEPAGY 60  
 DB 1 mhktasqrlfpgpsyqnklsimedstilsdwtcnankqkmydfscelyrmsytfepgy 60  
 QY 61 PVSESLARAGFYTYGVNDKVKFCGGLMDNMKLGDSPIQKHQLYPSCSFIONLYVAS 120  
 DB 61 pveselarsagfyytygvndkvkfcgglmndmwlqgsdpsqkqklypscstfionlyvas 120  
 QY 121 LGSTSKNTSPMRNSFAHSLSPTLHSSLFSGSYSSLSPPNLNSRAVEDISSRTNPSYA 180

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Db 121 1gstsntspmrnsfahslsplshslsfgysisspmsplnsravedissrtrmpysa 180
Oy 181 MSTEARFLTYHMPFLTFLSPSELARAGFYTGPDRAVACFACGKLSNWEKPDAMSEH 240
Db 181 msteearflyhmpfltlflspselaragfytgpdvraclacgklsnwekpdamseh 240
Oy 241 RRRFPNCPFLNSLETFLRFSISNLSMOTHAARMKRFMYWPSVVPQFOLASAGFYVGR 300
Db 241 rrrfpncpflensletflrfsisnlsmqthaaarmctfmywpsvvpqfolasagfyygr 300
Oy 301 NDVYKFCDCGGLRCMESGDDPWYEHAKRPPRCFELIRMGKGFVDEIOGRPHLEOL 360
Db 301 ndvkcfcddcgglrcwesgddpwvehakwprcfelirmkgfvdelsgrphlleql 360
Oy 361 STSTTGENADPPILHFGPCESSSEDVAMNMTPVYKSALEMGFNBDLYKQVOSKILTT 420
Db 361 ststtgeenadpplilhfgpesssedavmmtcvvksalemgfnrdlvkqvskiltt 420
Oy 421 GENYKTVNDIVSALLNAEDEKREERKEKQAEEMASDDSLIRKRNALFOQLTCVPLTD 480
Db 421 genyktvndivsallnaedekreerekqaeemasddslirkrnallfqqltcvpltd 480
Oy 481 NLKANVINKQEHDIKOKTOIPLOARELIDTILVKGMAANIFKNCLEIDSTLYKNLF 540
Db 481 nlkanvinkqehdilkqtkipqarelidtlvkgnaaanifkncleidslyknlf 540
Oy 541 VDKMKYITPDEVGSLSEBOLRLQEFRTCKVMDKEVSVFIPCGHLVWCECAPSLR 600
Db 541 vdkmkyitpdevsgslseeglrllqeerlckvmdkevsvfipcghlvwcgecapslr 600
Oy 601 KCPICRGITKGTVRTFLS 618
Db 601 kpicrgitkgtvrtfls 618

RESULT 3
AAV33998
ID AAV33998 standard; Protein: 618 AA.
XX
XX AAV33998;
XX
XX 26-NOV-1999 (first entry)
XX
XX Human cellular inhibitor of apoptosis-1 sequence.
XX
XX Cellular inhibitor of Apoptosis-1; antisense; diagnostic; therapeutic;
XX C-IAP-1; prophyllaxis; infection; inflammation; tumor formation.
XX
XX Homo sapiens.
XX
XX US5958772-A.
XX
XX 28-SEP-1999.
XX
XX 03-DEC-1998; 98US-0205204.
XX
XX 03-DEC-1998; 98US-0205204.
XX
XX (ISIS-) ISIS PHARM INC.
XX
XX Bennett CF, Cowsett LM, Ackermann EJ;
XX
XX WPI: 1999-561047/47.
XX
XX N-PSDB: AA222143.
XX
XX Antisense compounds complementary to Cellular Inhibitor of Apoptosis-1
XX useful for e.g. diagnostics, therapeutics, and as research reagents -
XX
XX Example 13: Columns 41-46; 32pp; English.
XX
XX The invention provides antisense compounds of 8-30 nucleotides that
XX inhibit the expression of human Cellular Inhibitor of Apoptosis-1
XX

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CC (C-IAP-1). The antisense compounds may be used for diagnostics,
CC therapeutics (for modulating the expression of C-IAP-1), prophylaxis
CC (e.g. to prevent or delay infection, inflammation or tumor formation),
CC as research reagents (e.g. to distinguish between members of a biological
CC pathway) and in kits. The present sequence represents the human cellular
CC inhibitor of apoptosis-1.
XX
XX Sequence 618 AA:
XX
XX Query Match 100.0%; Score 3277; DB 20; Length 618;
XX Best local similarity 100.0%; Pred. No. 1.3e-285;
XX Matches 618; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
Oy 1 MHKTSORLFPGPSONIKSJMDESTILSDWTNSNKKMYDPSCFLRMSTYTPFAGV 60
Db 1 mhktasgrlfpgpsygnlksamedstllsdwtnskmydpscflyrmstyslfpagv 60
Oy 61 PVSESLARAGFYTGYNKXKVCFCGGLMDNMKLGDSPIQKHQIYPCSPIONLVAS 120
Db 61 pvsestlaragfytgynkvkcfcgglmdnmkldgspiqkhqiypscpiqlnvass 120
Oy 121 LGSTSKNTSPMRNSFAHSLSPLEHSSLPSCSYSSLSPNLNSRAVEDISSKRTNPTSYA 180
Db 121 lgstskntspmrnsfahslsplshslsfgysisspmsplnsravedissrtrmpysa 180
Oy 181 MSTEARFLTYHMPFLTFLSPSELARAGFYTGPDRAVACFACGKLSNWEKPDAMSEH 240
Db 181 msteearflyhmpfltlflspselaragfytgpdvraclacgklsnwekpdamseh 240
Oy 241 RRRFPNCPFLNSLETFLRFSISNLSMOTHAARMKRFMYWPSVVPQFOLASAGFYVGR 300
Db 241 rrrfpncpflensletflrfsisnlsmqthaaarmctfmywpsvvpqfolasagfyygr 300
Oy 301 NDVYKFCDCGGLRCMESGDDPWYEHAKRPPRCFELIRMGKGFVDEIOGRPHLEOL 360
Db 301 ndvkcfcddcgglrcwesgddpwvehakwprcfelirmkgfvdelsgrphlleql 360
Oy 361 STSTTGENADPPILHFGPCESSSEDVAMNMTPVYKSALEMGFNBDLYKQVOSKILTT 420
Db 361 ststtgeenadpplilhfgpesssedavmmtcvvksalemgfnrdlvkqvskiltt 420
Oy 421 GENYKTVNDIVSALLNAEDEKREERKEKQAEEMASDDSLIRKRNALFOQLTCVPLTD 480
Db 421 genyktvndivsallnaedekreerekqaeemasddslirkrnallfqqltcvpltd 480
Oy 481 NLKANVINKQEHDIKOKTOIPLOARELIDTILVKGMAANIFKNCLEIDSTLYKNLF 540
Db 481 nlkanvinkqehdilkqtkipqarelidtlvkgnaaanifkncleidslyknlf 540
Oy 541 VDKMKYITPDEVGSLSEBOLRLQEFRTCKVMDKEVSVFIPCGHLVWCECAPSLR 600
Db 541 vdkmkyitpdevsgslseeglrllqeerlckvmdkevsvfipcghlvwcgecapslr 600
Oy 601 KCPICRGITKGTVRTFLS 618
Db 601 kpicrgitkgtvrtfls 618

RESULT 4
AAV19583
ID AAV19583 standard; Protein: 618 AA.
XX
XX AAV19583;
XX
XX 02-SEP-1997 (first entry)
XX
XX Human apoptosis inhibitor H1AP-2.
XX
XX Apoptosis inhibitor; H1AP-2; HIV; AIDS; neurodegeneration;
XX myelodysplastic syndrome; ischemia; myocardial infarction; stroke;
XX reperfusion injury; toxin-induced liver disease; gene therapy;
XX
XX
XX

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CC liver nasopharynx, thyroid, central nervous system, prostate, colon,  
CC rectum, cervix or endometrium, particularly to increase their sensitivity  
CC to chemotherapeutic agents. High levels of the IAP or NAIP proteins are  
CC detected in many cancers and are associated with poor prognosis.  
CC resistance to chemotherapeutic agents and mutations in p53 (11, 15  
CC suggested that wild-type p53 suppresses transcription of the IAP or NAIP  
CC genes). Transgenic animals are used for testing the effects of antisense  
CC oligonucleotides and for screening for the inhibitors.

XX Sequence 618 AA:

Query Match 99.1%; Score 3247; DB 19; Length 618;

Best Local Similarity 99.4%; Pred. No. 7,2e-287;

Matches 614; Conservative 0; Mismatches 4; Indels 0; Gaps 0;

```
QY 1 MHKTSQRLFPQPSYONIKSIEMDSTLLSDMTNSKQKMYDPSCELYRMSTYSPFAGV 60
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 1 mktasqllppspayqniksimeclsdwunskqkmydpscelymstyscpagv 60
QY 61 PVSEKSLARAGFYTGVDKVKCFCCGLMDNKKLGDSPIQKHKOLYPCSF10NLVSAS 120
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 61 pvserslaragfytgvndkvkcfccglmdnwkldgsplqkhkqlypscsf1qnlvsas 120
QY 121 LGSTSKNTSPMRNSFAHSLSPTEHSSLFSGSYSLSPNPLNSRAVEDISSRTNPYSYA 180
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 121 lgstskntspmrnsfahslspthesslfsqsysslpnpnlnsravedissrtnpysya 180
QY 181 MSTEERARFLUTYHMPPLTFLLSPSELARAGFYTGCDRVACFACGCKLSNWEPRKDDMSPH 240
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 181 msteearfllythmwppltfllspselaragfytgpcdractacgklsnweprkddamseh 240
QY 241 RHHFNCPEFLFENSLETRFESISLSMOTHAARMRTFMVPSVYVOPEDLASGFPYVGR 300
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 241 rhhfncpelfensletrfesislsmtqhaarmrtfmvpsvypvpedlasgfyvgr 300
QY 301 NDVVKCFCCDGLRCWESGDPAWEHAKWFPKCEFLIRMKQGFVDEIOGRYPHLEQL 360
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 301 ndvkcfcfccdglrcwesgdpavehakwfpkcelirmkqgefvdelqgrphlleql 360
QY 361 STSDTTGEENADPPIIHFGPGESSSDAVMMNTPVVKSALFEMGFNRDLVKOTVOSKILT 420
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 361 stsdttgeenadppihfpgesssdavmmntpvvksallemgfndrlvkqvtlskilt 420
QY 421 GENVYMDIVSALLNDEKREBEKQAEEMASDDLSLRKRMALFQOLTCVPLTD 480
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 421 genytmdivsallnedekekekaemasddlslrkrmalfqoltcvpltd 480
QY 481 NILKANVINRQEHDIQKQTOYLOAKRELDTILVKGAAANIFKNCLEKIDSTLYKNLF 540
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 481 nilkanvinrqedhdiqkqtcqldpqrrelclvwkgaanaalrkncleakidstlyknlf 540
QY 541 VDKNMKYIPTEDVSGLSLEBOLRLQEBRTKVCMDKEVSVVTFPGHLLVVCQCAPSLR 600
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 541 vdknmkyiptedvsglslebolrlqebtrkvcmdkevsvvtfpgchlvcqcapslr 600
QY 601 KCPICRGILKGTVRTFLS 618
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 601 kpicrgilkgtrtfls 618
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RESULT 6

ID AAM13555 standard; Protein: 612 AA.

XX AAM13555;

XX 22-JUL-1997 (first entry)

XX Murine c-IAP.

XX IAP: inhibitor; apoptosis; RING finger domain; restinosis;

KW myocardial infarction; nephritis; HIV.

XX Mus musculus.

XX M09706182-A1.

XX 20-FEB-1997.

XX 06-AUG-1996; 96WO-US12860.

XX 08-DEC-1995; 95US-0569749.

XX 08-AUG-1995; 95US-0512946.

XX (TULA-) TULARIX INC.

XX Goeddel DV, Rothe M;

XX WPL; 1997-154209/14.

XX N-PSDB; AAT61592.

XX Nucleic acids encoding cellular inhibitor of apoptosis proteins

XX useful for apoptosis regulation in cells to reduce or increase

XX apoptosis and for pharmacological screening

XX Disclosure: Page 28-29; 35pp; English.

XX The human cellular inhibitor of apoptosis proteins (c-IAP1/2

XX AAT61590/761591) comprise a series of defined structural domain

XX repeats and/or a RING finger domain; in particular, at least two of

XX a first domain repeat (AAM13547 or AAM13548), a second domain repeat

XX (AAM13549 or AAM13550), and a third domain repeat (AAM13551 or AAM13552)

XX and/or a RING finger domain (AAM13553 or AAM13554), or a consensus

XX sequences derived from these human genes.

XX The nucleic acid is used for recombinant prodn. of human cellular

XX inhibitor of apoptosis protein which modulates apoptosis

XX regulation. The nucleic acids are useful in therapies where

XX increased cell-specific apoptosis is desired, e.g. in restinosis,

XX inflammatory disease states, myocardial infarction, glomerulonephritis,

XX nephritis, transplant rejection and infectious diseases, e.g. HIV.

XX they can also be used in conditions requiring a reduction in

XX apoptosis.

XX Sequence 612 AA:

Query Match 83.2%; Score 2728; DB 18; Length 612;

Best Local Similarity 83.4%; Pred. No. 1.4e-239;

Matches 517; Conservative 45; Mismatches 48; Indels 10; Gaps 6;

```
QY 1 MHKTSQRLFPQPSYONIKSIEMDSTLLSDMTNSKQKMYDPSCELYRMSTYSPFAGV 60
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 1 mktasqrlfpgpysqniksimeclsdwunskqkmydpscelymstyscpagv 60
QY 61 PVSEKSLARAGFYTGVDKVKCFCCGLMDNKKLGDSPIQKHKOLYPCSF10NLVSAS 120
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 61 pvserslaragfytgvndkvkcfccglmdnwkldgsplqkhkqlypscsf1qnlvsas 120
QY 121 LGSTSKNTSPMRNSFAHSLSPTEHSSLFSGSYSLSPNPLNSRAVEDISSRTNPYSYA 180
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 121 lgstskntspmrnsfahslspthesslfsqsysslpnpnlnsravedissrtnpysya 180
QY 181 MSTEERARFLUTYHMPPLTFLLSPSELARAGFYTGCDRVACFACGCKLSNWEPRKDDMSPH 240
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 181 msteearfllythmwppltfllspselaragfytgpcdractacgklsnweprkddamseh 240
QY 241 RHHFNCPEFLFENSLETRFESISLSMOTHAARMRTFMVPSVYVOPEDLASGFPYVGR 300
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 241 rhhfncpelfensletrfesislsmtqhaarmrtfmvpsvypvpedlasgfyvgr 300
QY 301 NDVVKCFCCDGLRCWESGDPAWEHAKWFPKCEFLIRMKQGFVDEIOGRYPHLEQL 360
   ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db 301 ndvkcfcfccdglrcwesgdpavehakwfpkcelirmkqgefvdelqgrphlleql 360
QY 361 STSDTTGEENADPPIIHFGPGESSSDAVMMNTPVVKSALFEMGFNRDLVKOTVOSKILT 418
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Db      354  stddpgeenadpvtelvhfpgpe--ssedvymmtlpvkaalemgfstralvtgvtqql 412
      419  TTGENYKTVNDIVSALLNADEKREBEKEQAEMASDDSLIRKRNMLFOOLTCVLP 478
      413  atgenyrtvndivsvllnaederreekerqteemaagdsllrkrmalfqqlthvlp 472
      479  LDNLKAVYINKQEHDIKQKTOIPLOARELIDTLVKGNAANIRKNCLEIDSTLYKN 538
      473  ldnllaesvltkqghdlttrkqtqjprqarelldcvlvkgnaaanlfknsldstlyen 532
      539  LFVDKNMKYIPTEBVSGLSLEBOLRLQEBPTCKYQMDREVSVFIPCGHLVVCQECAPS 598
      533  lfveknmkypipdedvsglsleegllrrlqgeertckvcmdevslvflpcghlvvcqecaps 592
      599  LRKCPICRGIIKGTVPFELS 618
      593  lrkcplcrgrlikgtvtrflfs 612

RESULT 7
AAW69299
ID      AAW69299 standard; Protein: 612 AA.
XX
AC      AAW69299;
XX
DT      13-NOV-1998 (first entry)
XX
DE      Murine HIAP-2 protein.
XX
KM      Inhibitor of apoptosis protein; apoptosis enhancer; NAIP polypeptide;
KN      proliferative disease; IAP; therapy; cancer; mouse; HIAP-2 protein.
XX
OS      Mus sp.
XX
PN      WO9835693-A2.
XX
PD      20-AUG-1998.
XX
PF      13-FEB-1998; 98MO-1B0781.
XX
PR      13-FEB-1997; 97US-0800929.
XX
PA      (UYOT-) UNIV OTTAWA.
XX
PI      Baid S, Korneluk R, Liston P, Mackenzie AE, Pratt C;
PI      Tsang B;
XX
DR      MPI: 1998-467164/40.
DR      N-PSDB: AAV55043.
XX
PT      Inducing apoptosis in proliferative mammalian cells with inhibitor
PT      of IAP or NAIP polypeptide - also methods for prognosis based on
PT      presence of IAP and NAIP, specifically applied to cancers involving
PT      p53 mutations
XX
PS      Disclosure: fig 6; 147p; English.
XX
XX      This sequence is the murine HIAP-2 protein, which is an inhibitor of
CC      apoptosis protein (IAP), and can be used in the method of the invention.
CC      The method is for enhancing apoptosis in cells from a mammal with
CC      proliferative disease by treatment with a compound that inhibits
CC      biological activity of an IAP or NAIP polypeptide. The inhibitor
CC      compounds are used to treat proliferative diseases, specially cancers of
CC      ovary, breast, pancreas, lymph nodes, skin, blood, lung, brain, kidney,
CC      liver, nasopharynx, thyroid, central nervous system, prostate, colon,
CC      rectum, cervix or endometrium, particularly to increase their sensitivity
CC      to chemotherapeutic agents. High levels of the IAP or NAIP proteins are
CC      detected in many cancers and are associated with poor prognosis.
CC      resistance to chemotherapeutic agents and mutations in p53 (it is
CC      suggested that wild-type p53 suppresses transcription of the IAP or NAIP
CC      genes). Transgenic animals are used for testing the effects of antisense
CC      oligonucleotides and for screening for the inhibitors.

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XX      XX
SO      Sequence      612 AA:
      Query Match      83.1%; Score 2724; DB 19; Length 612;
      Best Local Similarity 83.2%; Pred. No. 3,3e-239;
      Matches 516; Conservative 46; Mismatches 48; Indels 10; Gaps 6;

      1  MKHTASORLFPGPSYONIKRISIMEDSTILSDMTNSKQMKAYDSCETLYMSTYTFPAGV 60
      1  mktvsgqlggqlhnglkrimekrtlsnwtksaeekmfdsctelymstysfprgvg 60
      61  PVSESRAPAGRYTGVNDKVCFCGGLMDMKKIGSPLOKXKOLYPSCSPTOMLVAS 120
      61  pvsersatrgllytyvndkvkfcicgglmdmkkgvsgpexknhqypscstlvqlsas 120
      121  LGSSTKNTSPMRNSFAHSLSPTEHSSLSFGSYSLSPNPLNBRAVEDISSRTNPTSYA 180
      121  lgspskntspmrnsfahslsp-tehsslsfsgyslsplnplnbravedi-ssrmdpcasya 173
      181  MSTEBAERFLTYHMPPLNPLSPSELARAGRYIGPDRYACFACGKLSMWERDPMSEH 240
      174  msteearfltysmwpplspselaragfyyigpdrvacfacgklsnwepkddamseh 233
      241  RRRHPCFPLNSLETLEFSISNLQTHAAMRTFMWFSVPVQPEOLASAGFYVGR 300
      234  rrrhpcplfntletelfslnsmqthartrfllwppsvpvqpeolasagfyyvdr 293
      301  NDDVKGPCCGDLGKMGESGDPVWEHAKWPRCEFLIMKGOEVDIIGRYPHLLEQL 360
      294  nddvkgfcdcgdlgkmgsgdpwvehakwprceflimkgoevdeiigrphlleql 353
      361  STSDTITGERNADP--PIIHRCPCSSSDAVVMKNTPVYKSLMEGKRNRLVKOTVSKIL 418
      354  stsdtpgeenadpcevvhfpgpe--skdvvmnsfpvkaalemgfstralvtgvtqql 412
      419  TTGENYKTVNDIVSALLNADEKREBEKEQAEMASDDSLIRKRNMLFOOLTCVLP 478
      413  atgenyrtvndivsvllnaederreekerqteemaagdsllrkrmalfqqlthvlp 472
      479  LDNLKAVYINKQEHDIKQKTOIPLOARELIDTLVKGNAANIRKNCLEIDSTLYKN 538
      473  ldnllaesvltkqghdlttrkqtqjprqarelldcvlvkgnaaanlfknsldstlyen 532
      539  LFVDKNMKYIPTEBVSGLSLEBOLRLQEBPTCKYQMDREVSVFIPCGHLVVCQECAPS 598
      533  lfveknmkypipdedvsglsleegllrrlqgeertckvcmdevslvflpcghlvvcqecaps 592
      599  LRKCPICRGIIKGTVPFELS 618
      593  lrkcplcrgrlikgtvtrflfs 612

RESULT 8
AAW19586
ID      AAW19586 standard; Protein: 591 AA.
XX
AC      AAW19586;
XX
DT      02-SEP-1997 (first entry)
XX
DE      Mouse apoptosis inhibitor M-HIAP-2.
XX
XX      Apoptosis inhibitor; M-HIAP-2; HIV; AIDS; neurodegeneration;
KM      myelodysplastic syndrome; ischemia; myocardial infarction; stroke;
KM      reperfusion injury; toxin-induced liver disease; gene therapy;
XX      diagnosis.
XX
OS      Mus sp.
XX
XX
FH      Key      Location/Qualifiers
FT      Domain      25..92
FT      /label= BIR-1

```





Db 421 lnaedeireeereateekesnd1111rkmalfhltvclp1d5llaglineghd 480

QY 495 IIRKORTQIPIQARELIDTILVKGNAAMIFRKNCLKEIDSTLYKNLFVQKMKMYIPTEDVS 554

Db 481 vlkqktqtsiqareldl1l1vkgnaaivfmslqaaevlyehlfvqgdklylpteds 540

QY 555 GLSLEQRLRLQERTCKVCMDEKVSVPFPCGHLVVCQECAPSLRKCPCIRGCIKGVYR 614

Db 541 d1pveeq1rl1geertckvcmdeksivf1p1cghlvvcdeaps1rlkpc1stlxlgtvr 600

QY 615 TFLS 618

Db 601 tfls 604

RESULT 11

AAVS2703

ID AAVS2703 standard: Protein: 604 AA.

AC AAVS2703:

XX 26-JAN-2000 (first entry)

DT Human cellular inhibitor of apoptosis-2 protein.

DE Identification: genetic target; gene modulation; human;

XX antisense oligonucleotide; phosphorothioate; target validation;

KM nucleotide sequence-based technology; antisense drug discovery.

XX Homo sapiens.

OS

XX

PN W09553101-A1.

XX 21-OCT-1999.

PD 13-APR-1999; 99MO-US08268.

XX 13-APR-1998; 98US-0081483.

PR 28-APR-1998; 98US-0067638.

XX (ISIS-) ISIS PHARM INC.

PA Cowser LT, Baker BF, McNeil J, Freiler SM, Sasnor HM, Brooks DG;

PI Ohasi C, Wyatt JR, Borchers AH, Vickers TA;

XX MPI: 1999-620446/53.

DR N-PSDB: AA241005.

XX

PT Identifying compounds which modulate expression of nucleic acids, used

PT to provide compounds having defined physical, chemical or bioactive

PT properties, e.g. antisense activity

XX

PS Example 20: Page 197-202: 264pp: English.

XX

XX A method has been developed of defining a set of compounds that modulate

CC the expression of a target nucleic acid (tma) sequence via binding of

CC the compounds with the tma sequence. The method comprises generating a

CC library of virtual compounds in silico according to defined criteria,

CC and evaluating in silico the binding of the virtual compounds with the

CC tma according to defined criteria. Also described are: (1) a method of

CC defining a set of oligonucleotides (ONS) that modulate the expression of

CC a tma sequence via binding of the ONS with the tma sequence comprising

CC generating a library of virtual compounds in silico according to defined

CC criteria, and evaluating in silico the binding of the virtual ONS with

CC the tma according to defined criteria; and (2) a method of defining a

CC set of compounds that modulate the expression of a tma sequence via

CC binding of the compounds with the tma. The methods can be used for the

CC generation and identification of synthetic compounds having defined

CC physical, chemical or bioactive properties. Information gathered from

CC assays of such compounds is used to identify nucleic acid sequences that

CC are tractable to a variety of nucleotide sequence-based technologies,

CC e.g. antisense drug discovery and target validation. AA240852 to

CC AA241220, and AAVS2701 to AAVS2706, represent sequences used in the

CC exemplification of the present invention.

XX

XX Sequence 604 AA:

Query Match 71.8%; Score 2353; DB 20; Length 604;

Best Local Similarity 72.8%; Pred. No. 2,1e-205;

Matches 440; Conservative 71; Mismatches 87; Indels 6; Gaps 5;

QY 20 SIMEDSTILSDWTNS-NKOKMKYDPSCELYRMSTYSTRPAGVPVSEKSLARAGFYTYGVN 78

Db 2 n1vens1f1sn1mk1sant1f1kyl1scl1ym1st1f1p1agvp1s1ar1agf1y1t1gvn 61

QY 79 DKVACFCGGLMLDNMKTGSP1OKHKOLYPCSCFTIONLVSA-SLGSTYSKNTSP--MRNSF 135

Db 62 dkvcfcfcgglmldnmkrgdsp1ekhk1ypscrf1ygs1nsvn1la1sq1clfp1s1vtns- 120

QY 136 AHSLSPTEHSLFSGSYSSLSPPLNSRAVEDISSRTPNPYSAMSTEARFLTYHMP 195

Db 121 thsl1p1gt1ensy1f1rg1ys1nsp1p1n1s1rang1d1f1s1m1s1y1hc1am1nen1ar1l1t1f1q1w 180

QY 196 LTFPLSPSLARAGFYTYIGCDRACVACFACGGKLSMPEPKDAMSEHRRHFPNCFLENSL- 254

Db 181 ltf1p1s1p1s1l1ar1agf1y1t1g1c1d1r1a1c1v1a1c1f1a1c1g1k1s1n1w1e1p1k1d1a1m1s1e1h1r1h1f1k1o1p1f1e1n1d1q 240

QY 255 ETIARFSISNLSMGTNHAARMRTFMPSVPVPEBOLASGFYTYGRBDYKPCCGCGH 314

Db 241 d1s1r1y1s1n1s1m1g1t1n1h1a1r1f1k1f1m1p1s1v1p1e1q1a1a1s1g1f1y1g1n1s1d1d1k1c1c1d1g1r 300

QY 315 CWESGDQPMVFEHAKMPPRCEPLINMKGOEFDVDEIGRYPHILDELSTSPTEENADP 374

Db 301 cwesgdqpmvfeh1akm1pp1r1c1e1p1l1n1m1k1g1o1e1f1d1v1d1e1i1g1r1y1p1h1i1l1d1e1l1s1t1s1p1t1e1e1n1a1d1p 360

QY 375 ITHRGPGSSSDANVMNTPVYKSKALEGFRDLYKQYOSKILTGENKTYNDIYSL 434

Db 361 i1t1h1r1g1p1g1s1s1d1a1n1v1m1n1t1p1v1y1k1s1k1a1l1e1g1f1r1d1y1k1o1s1k1i1l1t1g1e1n1k1t1y1n1d1i1y1s1l 420

QY 435 LNADEKREBEKKEKQAEKASDDLSLRKNMALFOQLTCVPLIDMLKANYINKOEND 494

Db 421 lnaedeireeereateekesnd1111rkmalfhltvclp1d5llaglineghd 480

QY 495 IIRKORTQIPIQARELIDTILVKGNAAMIFRKNCLKEIDSTLYKNLFVQKMKMYIPTEDVS 554

Db 481 vlkqktqtsiqareldl1l1vkgnaaivfmslqaaevlyehlfvqgdklylpteds 540

QY 555 GLSLEQRLRLQERTCKVCMDEKVSVPFPCGHLVVCQECAPSLRKCPCIRGCIKGVYR 614

Db 541 d1pveeq1rl1geertckvcmdeksivf1p1cghlvvcdeaps1rlkpc1stlxlgtvr 600

QY 615 TFLS 618

Db 601 tfls 604

RESULT 12

AAVS3997

ID AAVS3997 standard: Protein: 604 AA.

AC AAVS3997:

XX 26-NOV-1999 (first entry)

DE Human cellular inhibitor of apoptosis-2 sequence.

XX

XX Cellular inhibitor of Apoptosis-2; antisense; diagnostic; therapeutic;

KM c-1A-2; prophylaxis; infection; inflammation; tumor formation.

XX

OS Homo sapiens.

XX

PN US5958771-A.

XX 28-SEP-1999.

PD







Tue Jan 8 08:23:28 2002

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